Amendments to the Claims

Please amend Claims 32-34, 37-39, 41, 43, 44, 46, 52 and 53-54.

Please add Claim 57.

The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Original) A method of characterizing a multi-determinant metabolic phenotype, wherein a plurality of phenotypic determinants are identified as corresponding to respective metabolic characteristics, said method comprising:

   a. administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;

   b. detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and

   c. characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

2. (Original) The method of claim 1 which further comprises a step i) after step b): i) quantifying a ratio of respective detected metabolites for each of said metabolic pathways in said biological sample.

3. (Original) The method of claim 2, wherein said ratio is selected from the group consisting of concentration ratio, molar ratio, chiral ratio, ratio of area under the curve and signal peak height ratio.

4. (Original) The method of claim 1 wherein said probe substrate is at least one probe substrate known to be metabolized by said metabolic pathway.

5.   (Original) The method of claim 4, wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.

6.   (Original) The method of claim 1, wherein said step b) and/or c) is effected using an affinity complexation agent specific to each of said metabolites.

7.   (Original) The method of claim 6, wherein said affinity complexation agent is an antibody.

8.   (Original) The method of claim 7, wherein said antibody is a monoclonal antibody.

9.   (Original) The method of claim 7, wherein said antibody is a polyclonal antibody.

10.   (Original) The method of claim 6, wherein said affinity complexation agent is a molecular imprinted polymer.

11.   (Original) The method of claim 6, wherein said affinity complexation agent is an aptmer.

12.   (Original) The method of claim 6, wherein said affinity complexation agent is a receptor.

13.   (Original) The method of claim 6, wherein said affinity complexation agent is an anticalin.

14.   (Original) The method of claim 6 further comprising a ligand binding assay.

15.   (Original) The method of claim 14 wherein said ligand binding assay is selected from the group consisting of immunoassay, enzyme-linked immunosorbent assay (ELISA), microarray formatted immunoassay and microarray formatted ELISA.

16.   (Original) The method of claim 14, wherein said ligand binding assay is a rapid immunoassay (Dipstick assay).

17.   (Original) The method of claim 16, wherein said rapid immunoassay is based on Rapid Analyte Measurement Platform (RAMP) technology.

18.   (Original) The method of claim 16, wherein said rapid immunoassay is based on light–emitting immunoassay technology.

19.   (Original) The method of claim 14 wherein said ligand binding assay is performed with a biosensor.

20.   (Original) The method of claim 19 wherein said biosensor is an immunosensor.

21.   (Original) The method of claim 19 wherein the means of detection of said biosensor is an electrochemical sensor.

22.   (Original) The method of claim 19, wherein the means of detection of said biosensor is an optical sensor.

23.   (Original) The method of claim 19, wherein the means of detection of said biosensor is a microgravimetric sensor.

24.   (Original) The method of claim 23, wherein said microgravimetric sensor is a quartz crystal microbalance (QCM).

25. (Original) The method of claim 1, wherein step b) is effected using a qualitative detection instrument.

26. (Original) The method according to claim 1, wherein each of said plurality of phenotypic determinants of said multi-determinant metabolic phenotype is an enzyme-specific determinant.

27. (Original) The method according to claim 26 wherein said multi-determinant metabolic phenotype is comprised of at least one determinant indicative of an individual's metabolic capacity for at least one drug metabolizing enzyme.

28. (Original) The method of claim 27 wherein the said at least one drug metabolizing enzyme is selected from the group consisting of CYP1A2, N-acetyltransferase-1 (NAT-1), N-acetyltransferase-2 (NAT-2), CYP2D6, CYP2A6, CYP2E1, CYP3A4, CYP2C9, CYP2C19, UGTs, GSTs, and SUT.

29. (Original) The method of claim 2, wherein step a) is effected using a plurality of probe substrates and wherein each probe substrate is specific to at least one metabolic pathway of interest.

30. (Original) The method of claim 29, wherein said multi-determinant metabolic phenotype is characterized according to the method comprising:
    a.   administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;
    b.   detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and

c. characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

31. (Original) A method of using a multi-determinant metabolic phenotype to select a drug treatment regimen for an individual, said method comprising, comparing a metabolic profile of a candidate drug with said multi-determinant metabolic phenotype of said individual, and selecting said candidate drug for use in said treatment regimen for said individual when said multi-determinant metabolic phenotypic is indicative of a phenotype having metabolic efficiency for said candidate drug.

32. (Currently Amended) ~~The~~ A method of <u>using a multi-determinant metabolic phenotype to select a drug treatment regimen for an individual, said method comprising comparing a metabolic profile of a candidate drug with said multi-determinant metabolic phenotype of said individual, wherein said multi-determinant metabolic phenotype is characterized according to the method of Claim 1, and selecting said candidate drug for use in said treatment regimen for said individual when said multi-determinant metabolic phenotypic is indicative of a phenotype having metabolic efficiency for said candidate drug.</u> ~~claim 31 wherein said multi-determinant metabolic phenotype is characterized according to the method comprising:~~

~~a. administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~

~~b. detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~

~~c. characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

33. (Currently Amended) A method of using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said multi-determinant metabolic phenotype of said individual is <u>characterized</u> ~~determined~~; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon.

34. (Currently Amended) ~~The~~ <u>A</u> method of <u>using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said multi-determinant metabolic phenotype of said individual is characterized according to the method of Claim 1; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon.</u> ~~claim 33 wherein said multi-determinant metabolic phenotype is determined according to the method comprising:~~

~~a.   administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~

~~b.   detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~

~~c.   characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

35. (Original) The method of claim 33, wherein said drug treatment is selected from a class or genus of compounds with similar metabolic profiles.

36. (Original) The method of claim 35 wherein said drug treatment regimen is selected according to the method comprising:

a. administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;

b. detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and

c. characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

37. (Currently Amended) A method of The method of claim 36, using a multi-determinant metabolic phenotype to individualize a selected drug treatment regimen for an individual, wherein said drug treatment is selected from a class or genus of compounds with similar metabolic profiles; and wherein said multi-determinant metabolic phenotype of said individual is characterized according to the method of Claim 1; a safe and therapeutically effective dose of said drug treatment is determined for said individual based on said multi-determinant phenotype; and said dose for use in said selected treatment regimen for said individual is selected based thereon. wherein said multi-determinant metabolic phenotype is characterized according to the method comprising:

a) administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;

b) detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and

c) characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.

38. (Currently Amended) A method of treating an individual having a medical condition with a safe and therapeutically effective dose of a drug treatment known for use with said condition, said method comprising:

   a.   characterizing ~~determining~~ a multi-determinant metabolic phenotype of said individual; and

   b.   administering a safe and therapeutically effective dose of at least one compound known for treating said condition, wherein said at least one compound known for treating said condition has a metabolic profile corresponding to said individual's metabolic phenotype for said at least one compound as represented by said multi-determinant metabolic phenotype.

39.   (Currently Amended) ~~The~~ A method of <u>treating an individual having a medical condition with a safe and therapeutically effective dose of a drug treatment known for use with said condition, said method comprising:</u> ~~claim 38, wherein said multi-determinant metabolic phenotype is characterized according to the method comprising:~~

   a.   <u>characterizing a multi-determinant metabolic phenotype of said individual according to the method of Claim 1; and</u> ~~administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~

   b.   <u>administering a safe and therapeutically effective dose of at least one compound known for treating said condition, wherein said at least one compound known for treating said condition has a metabolic profile corresponding to said individual's metabolic phenotype for said at least one compound as represented by said multi-determinant metabolic phenotype.</u> ~~detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~

   ~~c.   characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

40.   (Original) A method of selecting a treatment for an individual corresponding to said individual's multi-determinant metabolic phenotype, said method comprising:

   a.   characterizing a multi-determinant metabolic phenotype of said individual;

b.   identifying a treatment from a group of candidate treatments that corresponds to said individual's multi-determinant metabolic phenotype; and

c.   selecting said treatment.

41.   (Currently Amended) ~~The~~ A method of <u>selecting a treatment for an individual corresponding to said individual's multi-determinant metabolic phenotype, said method comprising:</u> ~~claim 40 wherein said multi-determinant metabolic phenotype is determined according to the method comprising:~~

a.   <u>characterizing a multi-determinant metabolic phenotype of said individual according to the method of Claim 1;</u> ~~administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~

b.   <u>identifying a treatment from a group of candidate treatments that corresponds to said individual's multi-determinant metabolic phenotype; and</u> ~~detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~

c.   <u>selecting said treatment.</u> ~~characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

42.   (Original) A method of screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of a candidate drug treatment, said method comprising:

a.   characterizing a multi-determinant metabolic phenotype of each of said plurality of individuals;

b.   identifying those individuals having a metabolic phenotype characterized as effective for metabolizing said candidate drug treatment.

43. (Currently Amended) ~~The~~ <u>A</u> method of <u>screening a plurality of individuals for participation in a drug treatment trial assessing the therapeutic effect of a candidate drug treatment, said method comprising:</u> ~~claim 42 wherein said multi-determinant metabolic phenotype is determined according to the method comprising:~~

    a.   <u>characterizing a multi-determinant metabolic phenotype of each of said plurality of individuals according to the method of Claim 1; and</u> ~~administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~

    b.   <u>identifying those individuals having a metabolic phenotype characterized as effective for metabolizing said candidate drug treatment.</u> ~~detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~

    ~~c.   characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

44. (Currently Amended) An assay system for detecting the presence of multiple determinant-specific metabolites in a biological sample obtained from an individual treated with at least one probe substrate specific for metabolic pathways of said metabolites; said system comprising:

    a.   means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;

    b.   means for detecting presence of said metabolites bound to said affinity complexation agents; and

    c.   means for quantifying ratios of said metabolites to provide corresponding pheontypic determinants;

    wherein said phenotypic determinants provide a <u>multi-determinant</u> metabolic phenotype ~~profile~~ of said individual.

45. (Original) The assay system of claim 44, wherein said probe substrate is other than an inducer or inhibitor of said metabolic pathway.

46. (Currently amended) An assay system for detecting the presence of multiple determinant-specific metabolites in a biological sample obtained from an individual treated with at least one probe substrate specific for metabolic pathways of said metabolites, said system comprising:

   a) means for receiving said biological sample, including a plurality of affinity complexation agents contained therein;

   b) means for detecting presence of said metabolites bound to said affinity complexation agents; and

   c) means for quantifying ratios of said metabolites to provide corresponding phenotypic determinants;

   wherein said phenotypic determinants provide a multi-determinant metabolic phenotype profile of said individual and said steps b) and/or c) are effected according to the method of claim 6.

47. (Original) The assay system of claim 44 wherein said means for receiving said biological sample is a multi-well microplate including said plurality of affinity complexation agents in each well.

48. (Original) The assay system of claim 47 wherein said plurality of affinity complexation agents are bound to each well in an array-based format.

49. (Original) The assay system of claim 48 wherein said means for detecting said presence of said metabolites bound to said binding agents is a charge-coupled device (CCD) imager.

50. (Original) The assay system of claim 44 wherein said means for said quantifying ratios of said metabolites is a densitometer.

51. (Original) A method of using a multi-determinant metabolic phenotype of claim 1 for determining a combination drug therapy wherein an individual's phenotype is indicative of a fast metabolizer, and a corresponding inhibitor is selected for combined treatment with a drug to improve the therapeutic effect thereof in said individual.

52. (Currently Amended) A method of diagnosing a disease or condition associated with altered function in a drug metabolizing enzyme(s) by ~~determining~~ characterizing an individual's multi-determinant metabolic ~~phenotyping~~ phenotype.

53. (Currently amended) ~~The~~ A method of diagnosing a disease or condition associated with altered function in a drug metabolizing enzyme or enzymes by determining an individual's multi-determinant metabolic phenotype ~~claim 52~~ wherein said multi-determinant metabolic phenotype is characterized ~~determined~~ according to the method of Claim 1. ~~comprising:~~
   ~~a.   administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;~~
   ~~b.   detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and~~
   ~~c.   characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.~~

54. (Currently Amended) A method of determining the ability of a compound to affect ~~effect~~ the function of a drug metabolizing enzyme(s) *in vivo* whereby:

    a.   a multi-determinant metabolic phenotype of a biological organism is characterized ~~determined~~ according to the method of claim 1 prior to compound exposure;

    b.   said biological organism is exposed to said compound;

    c.   a multi-determinant metabolic phenotype of said biological organism is characterized ~~determined~~ according to the method of claim 1 after said compound exposure; and

    d.   a comparison of multi-determinant phenotypes characterized ~~determined~~ pre- and post- compound exposure is made, whereby a change in the multi-determinant phenotypes characterized ~~determined~~ post-compound exposure as compared to pre-compound exposure is indicative of said drug's ability to affect ~~effect~~ the function of the drug metabolizing enzyme(s) in said biological organism.

55.   (Original) Method of claim 54, wherein said biological organism is a mammal.

56.   (Original) Method of claim 55, wherein said mammal is a human.

57.   (New) An assay system for characterizing a multi-determinant metabolic phenotype, wherein a plurality of phenotypic determinants are identified as corresponding to respective metabolic characteristics, said assay system comprising:

    a.   means for administering to an individual a probe substrate specific to a metabolic pathway of each of said plurality of phenotypic determinants;

    b.   means for detecting metabolites of said metabolic pathways in a biological sample from said individual in response to said probe substrate; and

    c.   means for characterizing respective phenotypic determinants of said multi-determinant metabolic phenotype based on detected metabolites.